REMARKS

Claims 13-21 are pending and under examination. Applicant appreciates: 1) the Examiner's considering the references submitted with the December 6, 2000 Supplemental Information Disclosure Statement and returning an initialed copy the Form PTO-1449; 2) the Examiner's considering the full text articles of Reference Nos. 7, 30, 35-36 and 39; 3) the Examiner's acknowledgement of the Supplemental Declaration filed May 14, 2001; and 4) the withdraw of the objections to claims 13-21.

Rejection under 35 U.S.C. § 112, first paragraph

The rejection of claims 13-21 under 35 U.S.C. 112, first paragraph, is maintained. The Examiner states that the Glenn Declaration, applicant's arguments, and Exhibits B-M have been fully considered but they are not persuasive.

This rejection is respectfully traversed. Applicant submits that the Examiner has applied incorrect standard for the enablement analysis and in any case, the newly submitted *in vivo* data overcome the enablement rejection.

In vivo testing data is not *per se* required to enable use in humans

Much of the Examiner's rejection is based on the lack of *in vivo* data in the present case. However, established legal precedents make it clear that *in vivo* data is not *per se* required to enable methods of treatment including treatment of diseases or other conditions in humans. A case in point is *Ex parte Bhide*, 42 USPQ2d 1441 (Bd. Pat. App. & Int'f. 1996).

The claimed invention in *Ex parte Bhide* is directed to compounds that can be used as prenylation inhibitors. The examiner rejected the claims for the alleged lack of utility under 35 U.S.C. § 101 and nonenablement under 35 U.S.C. § 112, first paragraph, for a number of reasons including the lack of *in vivo* testing data. The Board affirmed the rejection on a new ground and made it clear that the examiner there used incorrect standard for the enablement analysis. *Ex parte Bhide*, 42 USPQ2d at 1448. Speaking to the "burden of proof" issue in the enablement analysis, the Court in *Ex parte Bhide* stated:

> A specification which contains a statement of the manner and process of using the invention in terms which correspond in scope to those used in defining the subject sought to be patented *must* be taken as in compliance with the "how to use' requirement of the

> first paragraph of 35 U.S.C. § 112 *unless* there is a reason to doubt the objective truth of the statement [italicize original and cites omitted].

Ex parte Bhide, 42 USPQ2d at 1447. As to the adequacy of using *in vitro* or *in vivo* data to overcome the non-enablement rejection, the Court in *Ex parte Bhide* stated:

> As *In re Langer* makes clear, a § 101 rejection may be overcome by suitable proofs indicating that the statement of utility and its scope as described in the specification are true. 503 F.2d 1391, 183 USPQ 27 297. The same is true for a rejection based on a failure of 'how to use' under 35 U.S.C. § 112, first paragraph. Thus, on different record, the Patent and Trademark Office might be able to find that applicants' claimed compounds are useful. While *in vitro* or *in vivo* tests would not be the only possible way to overcome our basis for questioning applicants' utility, *in vitro* or *in vivo* tests certainly would provide relevant evidence [italicize original and underline added].

Ex parte Bhide, 42 USPQ2d at 1448.

It is well established that human clinical trial is not required to show enablement of treatment including treatment of diseases or other conditions in humans. The Court in *In re Langer*, 183 USPQ 288, 298 (CCPA 1974) stated:

> Full scale clinical trials in humans, such as described in the Dental Abstracts reference (see note 16, supra), may be necessary to establish "commercial usefulness" in this technology. However, development of a product to the extent that it is presently commercially salable in the market place is not required to establish "usefulness" within the meaning of § 101. *citing In re Anthony*, 56 CCPA 1442, 414 F.2d 1383, 162 USPQ 594 (1969).

This is also recognized by the case cited in the Final Office Action, *i.e.*, *Ex parte Balzarini*, 21 USPQ2d 1892, 1897 (Bd. Pat. App. & Int'f. 1991).

In addition, the cited references, Benet and Rice, are not related to the presently claimed method which is based on the inhibition of prenylation of a viral protein. Benet concerns with the development of pharmaceuticals generally and Rice reviews discovery and *in vitro* development of AIDS antiviral drugs as biopharmaceuticals. As discussed in the previous Amendment, none of the target/inhibitory compound discussed in Rice involves inhibition of prenylation of a viral protein. The Examiner also cited Gibbs to support the non-enablement argument. The portion of Gibbs that cited by the Examiner, *i.e.*, pages 4-3, is Gibbs' own speculation and is not supported by any testing data, *in vitro* or *in vivo*. However, as recognized by the Court in *In re Langer*, one cannot apply different enablement standards to the claims under examination and the teachings of the cited prior art references. The *In re Langer* Court said:

> It is not proper for the Patent Office to require clinical testing in humans to rebut a prima facie case for lack of utility when the pertinent references which establish the prima facie case show in vitro tests and when they do not show in vivo tests employing standard experimental animals.

In re Langer, 183 USPQ at 297. Accordingly, the Examiner should not use Gibbs' speculative statement to show alleged non-enablement of the presently pending claims.

The presently claimed methods can be used to treat viral infection *in vivo*

Even assuming, *arguendo*, that *in vivo* testing data is required in the present case, the non-enablement rejection is overcome by the data shown in the GLENN DECLARATION II, which demonstrated that prenylation inhibitors FTI-277 and FTI-2153 can effectively inhibit HDV virion production *in vivo* at a concentration that is not toxic to the testing animals. In addition, various prenylation inhibitors such as FTI-277, R115777, and SCH66336 have been used in human clinical trials and some have advanced to phase II clinical trials, indicating that these inhibitors have past safety test of the human clinical trials (*See e.g.*, Alex et al., *Clin. Can. Res.*, 6:2318-2325 (2000) (Exhibit B); Kelland et al., *Clin. Can. Res.*, 6:3544-3550 (2001) (Exhibit C); Zujewski et al., *J. Clin. Oncol.*, 18:927-941 (2000) (Exhibit D); and Karp et al., *Curr. Opin. Oncol.*, 13:470-476 (2001) (Exhibit E)).

The "mimic of a prenyl group" defines a clear scope

The Examiner further alleged that applicant has failed to define a function which can be used to determine if a compound is encompassed within the recited "mimic of a prenyl group."

This rejection is respectfully traversed. Applicant submits, as discussed in the previous Amendment, the term "mimic of a prenyl group" defines a clear scope, *i.e.*, "a mimic of a prenyl group" should behave like a prenyl group, *e.g.*, farnesyl diphosphate, but cannot be used as a prenyl group donor in a functional prenylation reaction. There are numerous ways a mimic of a prenyl group can achieve its inhibitory function. One example is being a competitive inhibitor of a prenyl group donor. Another example is to be a modified prenyl group so that even though the mimic may be attached to a target protein by prenyltransferase, the presence of the modification in the mimic interferes with the usual function provided by attachment of a normal prenyl group to a target protein. In this embodiment, the mimic-modified protein no longer behaves as the same protein would when modified by a normal prenyl group

The Examiner's rejection on this ground is based on the Examiner's questioning of the objective truth of the applicant's statement in the specification that a mimic of a prenyl group can be used as a prenylation inhibitor and be used to treat viral infection. This rejection is without merit because the Examiner has not presented any reason to doubt the objective truth of the applicant's statement. *See Ex parte Bhide*, 42 USPQ2d at 1447. If the Examiner is concerned with the scope of this limitation, this is also unpermissible because the Examiner has not presented any evidence to show that different prenyl group mimics would behave differently and the different reactivities of the compounds are relevant to the claimed methods. *Id.* (stating that the examiner's rejection is incorrect because no evidence was cited by the examiner to show that any different reactivities would make some compounds useful and others not useful and a claim is not unpatentable under 35 U.S.C. § 101 or § 112, first paragraph, merely because compounds within its scope have different reactivities.).

CONCLUSION

Applicant submits that the rejection of claims 13-21 under 35 U.S.C. §112 has been overcome by the above remarks. Early allowance of the pending claims 13-21 are earnestly requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the

filing of this document to **Deposit Account No. 03-1952** referencing docket no. 240042052403. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: February 5, 2002 By: _____

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